EXHIBIT A

Electronically filed on March 4, 2014

Application No. 12/969,581
Attorney Docket No. 41977-701.201

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Patent Application of: Applicant: Stephen P.A. Fodor, et al. Serial No.: 12/969,581 Filed: December 15, 2010 Title: Digital Counting of Individual Molecules by Stochastic Attachment of Diverse Labels	Confirmation No.: 4473 Group Art Unit: 1636 Examiner: Channing S. Mahatan

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RESPONSE TO NON-FINAL OFFICE ACTION

Madam:

This correspondence responds to the Non-Final Office Action dated October 3, 2013. The shortened statutory period for response expired on January 3, 2014. The Response is submitted after the shortened statutory period for reply, therefore, an extension fee is required to enter this Amendment. Applicants request an Extension of Time under § 1.136; and this Response is accompanied by the payment of a two-month extension of time fee, thereby extending the time for response to March 4, 2013, with the inclusion of the extra day due to USPTO closure on March 3, 2014. Accordingly, this Response is timely filed. Reconsideration of the above-referenced application is respectfully requested in view of the following amendments and remarks.

AMENDMENTS TO THE CLAIMS:

1-25. (Cancelled)

26. (Currently Amended) A method for counting *n* wherein n is ~~the~~a number of molecules of a first target molecule that are present in a sample comprising: (a) attaching by a species-independent manner to each occurrence of the first target molecule a label from a set of diverse labels, wherein ~~said~~ the set comprises *m* different labels, thereby generating for each occurrence of the first target molecule, a new molecule that comprises a copy of the first target molecule and a label, wherein more than 90% of the new molecules have a label that is different from the labels on the other new molecules; (b) detecting each new molecule by detecting each label present on ~~a~~the new molecule; and (c) counting ~~the~~a number of new molecules, thereby counting the number of molecules of the first target molecule in the sample.

27. (Original) The method of claim 26 wherein ~~the~~a ratio of *m* to *n* is greater than 50.

28. (Original) The method of claim 26 wherein ~~the~~a ratio of *m* to *n* is greater than 100.

29. (Original) The method of claim 26 wherein ~~the~~a ratio of *m* to *n* is greater than 500.

30. (Original) The method of claim 26 wherein ~~the~~a ratio of *m to n* is greater than 1000.

31. – 38. (Cancelled)

39. (Currently Amended) A method comprising:

(a) combining a mixture comprising at least two distinct target nucleic acid molecules with a pool of nucleic acid label-tags, wherein ~~said~~the pool of nucleic acid label-tags comprises a plurality of nucleic acid label-tags with different sequences;

(b) attaching at least two ~~of said~~ nucleic acid label-tags from ~~said~~the pool of nucleic acid label-tags to the at least two ~~of said~~ distinct target nucleic acid molecules to obtain at least two label-tag-target nucleic acid molecules, wherein ~~said~~the distinct target nucleic acid molecules have different sequences from one another[[,]];

(c) amplifying at least a portion of ~~said~~the label-tag-target nucleic acid molecules, wherein an amplified portion of ~~said~~the label-tag-target nucleic acid molecules comprises at least a portion of said target nucleic acid molecule; and

(d) detecting an amplified product of step (c).

40. (Currently amended) The method of claim 39, wherein ~~said~~the attaching is stochastic.

41. (Currently amended) The method of claim 39, wherein ~~said the~~ distinct target nucleic acid molecules are known targets.

42. (Currently amended) The method of claim 39, wherein ~~said~~the nucleic acid label-tags are designed to bind to ~~said~~the distinct target ~~particular~~ nucleic acid ~~target~~ molecules.

43. (Currently amended) The method of claim 39, wherein an identity of ~~said~~the distinct target nucleic acid molecules is determined after the detecting step.

44. (Currently amended) The method of claim 39, wherein ~~said~~the nucleic acid label-tags ~~will~~may bind to any of ~~said~~the distinct target nucleic acid molecules.

45. (Currently amended) The method of claim 39, wherein ~~said~~the attaching occurs on both ends of at least one of ~~said~~the two distinct target nucleic acid~~s~~ molecules.

46. (Currently amended) The method of claim 39, wherein ~~said~~the detecting comprises hybridizing at least a portion of ~~said~~the label-tag-target nucleic acid molecules to a solid or semi-solid substrate.

47. (Currently amended) The method of claim 39, wherein ~~said~~ the detecting~~hybridizing~~ comprises hybridizing at least a portion of ~~said~~the target nucleic acid molecule to a solid or semi-solid substrate.

48. (Currently amended) The method of claim 39, wherein ~~said~~ the detecting~~hybridizing~~ comprises hybridizing at least a portion of ~~said~~the nucleic acid label-tag to a solid or semi-solid substrate.

49. (New) The method of claim 26, wherein the attaching of step (a) is stochastic.

50. (New) The method of claim 26, wherein the attaching of step (a) comprises ligation of the label to an occurrence of the first target molecule.

51. (New) The method of claim 26, wherein the attaching of step (a) comprises reverse transcription of an occurrence of the first target molecule.

52. (New) The method of claim 26, wherein the attaching of step (a) comprises use of the label for primer extension.

53. (New) The method of claim 26, wherein the first target molecule is a nucleic acid.

54. (New) The method of claim 26, wherein the first target molecule is RNA.

55. (New) The method of claim 54, wherein the RNA is mRNA.

56. (New) The method of claim 55, wherein the labels comprise an oligodT sequence.

57. (New) The method of claim 56, wherein the labels are attached to the molecules by hybridization of the oligodT sequence of the label to a polyA tail of the mRNA.

58. (New) The method of claim 26, wherein the first target molecule is DNA.

59. (New) The method of claim 26, further comprising fragmenting the occurrences of the first target molecule.

60. (New) The method of claim 59, wherein the occurrences of the first target molecule are fragmented prior to the attaching of step (a).

61. (New) The method of claim 59, wherein fragmenting the occurrences of the first target molecule comprises restriction enzyme digestion of the occurrences of the first target molecule.

62. (New) The method of claim 26, further comprising amplifying the new molecules.

63. (New) The method of claim 62, wherein amplifying comprises PCR.

64. (New) The method of claim 62, wherein amplifying comprises rolling circle amplification.

65. (New) The method of claim 26, wherein detecting the new molecule comprises detecting at least a portion of the copy of the first target molecule.

66. (New) The method of claim 26, wherein detecting the new molecule comprises detecting a junction formed between the label and the copy of the first target molecule.

67. (New) The method of claim 26, wherein detecting the new molecule comprises detecting at least a portion of the copy of the first target molecule and at least a portion of the label.

68. (New) The method of claim 26, wherein detecting the new molecule comprises conducting a sequencing reaction.

69. (New) The method of claim 68, wherein conducting the sequencing reaction comprises sequencing at least a portion of the copy of the first target molecule.

70. (New) The method of claim 68, wherein conducting the sequencing reaction comprises sequencing at least a portion of the label.

71. (New) The method of claim 68, wherein conducting the sequencing reaction comprises sequencing a junction formed between the label and the copy of the first target molecule.

72. (New) The method of claim 68, wherein conducting the sequencing reaction comprises sequencing at least a portion of the copy of the first target molecule and at least a portion of the label.

73. (New) The method of claim 26, wherein detecting the new molecule comprises hybridization of the new molecule to a solid support.

74. (New) The method of claim 73, wherein the solid support is an array.

75. (New) The method of claim 73, wherein the solid support comprises a plurality of probes.

76. (New) The method of claim 75, wherein a probe of the plurality of probes comprises a sequence that is complementary to at least a portion of the copy of the first target molecule.

77. (New) The method of claim 75, wherein a probe of the plurality of probes comprises a sequence that is complementary to at least a portion of the label.

78. (New) The method of claim 75, wherein a probe of the plurality of probes comprises a sequence that is complementary to a junction formed between the label and the copy of the first target molecule.

79. (New) The method of claim 75, wherein a probe of the plurality of probes comprises a sequence that is complementary to at least a portion of the label and at least a portion of the copy of the first target molecule.

80. (New) The method of claim 26, wherein the attaching of step (a) further comprises attaching labels to occurrences of one or more additional target molecules, wherein the first target molecule is different from the one or more additional target molecules.

81. (New) The method of claim 80, wherein the counting of step (c) further comprises counting a number of new molecules of the one or more additional target molecules, thereby counting a number of molecules of the one or more additional target molecules.

82. (New) The method of claim 80, wherein the one or more additional target molecules comprise 2 or more target molecules.

83. (New) The method of claim 80, wherein the one or more additional target molecules comprise 5 or more target molecules.

84. (New) The method of claim 80, wherein the one or more additional target molecules comprise 10 or more target molecules.

85. (New) The method of claim 80, wherein *m* different labels in the set of labels is constant.

86. (New) The method of claim 80, wherein the set of labels comprises multiple copies of the same label.

87. (New) The method of claim 86, wherein copies of a first label may attach to the occurrences of the first target molecule and the occurrences of the one or more additional target molecules.

88. (New) The method of claim 26, wherein the attaching of step (a) occurs on one end of an occurrence of the first target molecule.

89. (New) The method of claim 26, wherein the attaching of step (a) occurs on both ends of an occurrence of the first target molecule.

90. (New) The method of claim 26, wherein the label comprises an adaptor.

91. (New) The method of claim 26, wherein the label comprises a universal primer.

92. (New) The method of claim 80, wherein the label does not comprise a sequence that is specific to one species of target molecules.

93. (New) The method of claim 26, wherein the copy of the first target molecule is an occurrence of the first target molecule.

94. (New) The method of claim 26, wherein the copy of the first target molecule is a copy of an occurrence of the first target molecule.

95. (New) The method of claim 26, wherein the copy of the first target molecule is a complement or reverse complement of an occurrence of the first target molecule.

96. (New) The method of claim 39, wherein the attaching of step (b) occurs in a species-independent manner.

97. (New) The method of claim 39, wherein the attaching of step (b) occurs in a non-specific manner.

98. (New) The method of claim 39, wherein the pool of nucleic acid label-tags comprises multiple copies of a nucleic acid label-tag.

99. (New) The method of claim 98, wherein the copies of the nucleic acid label-tag may attach to copies of a first target nucleic molecule and copies of a second target nucleic acid molecule.

100. (New) The method of claim 39, wherein the attaching of step (b) comprises ligation of the label-tags to copies of the two distinct target nucleic acid molecules.

101. (New) The method of claim 100, wherein the copies of the two distinct target nucleic acid molecules are occurrences of the two distinct target nucleic acids molecules.

102. The method of claim 100, wherein the copies of the two distinct target nucleic acid molecules are copies of occurrences of the two distinct target nucleic acids molecules.

103. (New) The method of claim 100, wherein the copies of the two distinct target nucleic acid molecules are complements or reverse complements of occurrences of the two distinct target nucleic acids molecules.

104. (New) The method of claim 39, wherein the attaching of step (b) comprises reverse transcription of the two distinct target nucleic acid molecules.

105. (New) The method of claim 39, wherein the two distinct target nucleic acid molecules are RNA.

106. (New) The method of claim 105, wherein the RNA is mRNA.

107. (New) The method of claim 106, wherein the label-tags comprise an oligodT sequence.

108. (New) The method of claim 107, wherein the label-tags are attached to the two distinct target nucleic acid molecules by hybridization of the oligodT sequence of the label-tag to a polyA tail of the mRNA.

109. (New) The method of claim 39, wherein the two distinct target nucleic acid molecules are DNA.

110. (New) The method of claim 39, further comprising fragmenting the two distinct target nucleic acid molecules.

111. (New) The method of claim 110, wherein the two distinct target nucleic acid molecules are fragmented prior to the attaching of step (b).

112. (New) The method of claim 110, wherein fragmenting the two distinct target nucleic acid molecules comprises restriction enzyme digestion of the two distinct target nucleic acid molecules.

113. (New) The method of claim 39, wherein amplifying comprises PCR.

114. (New) The method of claim 39, wherein amplifying comprises rolling circle amplification.

115. (New) The method of claim 39, wherein detecting the amplified product comprises detecting at least a portion of the distinct target nucleic acid molecule.

116. (New) The method of claim 39, wherein detecting the amplified product comprises detecting at least a portion of the label-tag.

117. (New) The method of claim 39, wherein detecting the amplified product comprises detecting a junction formed between the label-tag and the distinct target nucleic acid molecule.

118. (New) The method of claim 39, wherein detecting the amplified product comprises detecting at least a portion of the distinct target nucleic acid molecule and at least a portion of the label.

119. (New) The method of claim 39, wherein the detecting of step (d) comprises conducting a sequencing reaction.

120. (New) The method of claim 112, wherein conducting the sequencing reaction comprises sequencing at least a portion of the distinct target nucleic acid molecule.

121. (New) The method of claim 112, wherein conducting the sequencing reaction comprises sequencing at least a portion of the label-tag.

122. (New) The method of claim 112, wherein conducting the sequencing reaction comprises sequencing a junction formed between the label-tag and the distinct target nucleic acid molecule.

123. (New) The method of claim 112, wherein conducting the sequencing reaction comprises sequencing at least a portion of the distinct target nucleic acid molecule and at least a portion of the label-tag.

124. (New) The method of claim 39, wherein detecting the amplifed product comprises hybridization of the amplified product to a solid support.

125. (New) The method of claim 124, wherein the solid support is an array.

126. (New) The method of claim 124, wherein the solid support comprises a plurality of probes.

127. (New) The method of claim 126, wherein a probe of the plurality of probes comprises a sequence that is complementary to at least a portion of the distinct target nucleic acid molecule.

128. (New) The method of claim 126, wherein a probe of the plurality of probes comprises a sequence that is complementary to at least a portion of the label-tag.

129. (New) The method of claim 119, wherein a probe of the plurality of probes comprises a sequence that is complementary to a junction formed between the label-tag and the distinct target nucleic acid molecule.

130. (New) The method of claim 126, wherein a probe of the plurality of probes comprises a sequence that is complementary to at least a portion of the label-tag and at least a portion of the distinct target nucleic acid molecule.

131. (New) The method of claim 39, further comprising determining a count of the at least two distinct target nucleic acid molecules based on the detection of the amplified product.

132. (New) The method of claim 131, wherein determining the count of the at least two distinct target nucleic acid molecules comprises determining the count of 5 or more distinct target nucleic acid molecules.

133. (New) The method of claim 131, wherein determining the count of at least two distinct target nucleic acid molecules comprises determining the count of 10 or more distinct target molecules.

134. (New) The method of claim 39, wherein the attaching of step (b) occurs on one end of the distinct target nucleic acid molecules.

135. (New) The method of claim 39, wherein the attaching of step (b) occurs on both ends of the distinct target nucleic acid molecules.

136. (New) The method of claim 39, wherein the label-tag comprises an adaptor.

137. (New) The method of claim 39, wherein the label-tag comprises a universal primer.

138. (New) The method of claim 39, wherein the label-tag does not comprise a sequence that is specific to one species of at least two distinct target nucleic acid molecules.

REMARKS

Status of the Claims

Claims 26-30 and 39-131 are pending. Claims 1-25 and 31-38 are cancelled. Claims 26-30 and 39-48 are currently amended. Claims 49-138 are new. Support for amendments and new claims can be found in the specification as filed. Applicants reserve the right to pursue the subject matter of the canceled claims in this or any other appropriate patent application. No new matter is added.

Interview Summary

Applicants greatly appreciate the courtesy that was extended by Examiner Mahatan during the interview conducted on February 27, 2014 with Vern Norviel and Stephen Fodor. During the interview, differences between certain references (e.g., Hug et al.) and the claimed invention were discussed. The Office and Applicants discussed proposed amendments, which have been incorporated into the currently pending claims.

Response to Rejections

112(b) Rejection of claims 5 and 7-10

Claims 5 and 7-10 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Without conceding the validity of the rejection, and solely to expedite prosecution, Applicants have cancelled claim 5 and 7-10, thereby rendering the rejection moot. Withdrawal of the rejection is respectfully requested.

103(a) Rejection of claims 1-4, 6, 17-23, and 26-48

Claims 1-4, 6, 17-23, and 26-48 are rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over Hug et al.

Without conceding the validity of the rejection, and solely to expedite prosecution, Applicants have cancelled claims 1-4, 6, 17-23 and 31-38 and have amended claim 26 to recite "(a)

attaching by a species-independent manner to each occurrence of the first target molecule a label from a set of diverse labels." As acknowledged by the Examiner in the interview conducted on February 27, 2013, as well as in the Office Action dated October 3, 2013, at p. 5, line 7, Hug et al. does not teach labeling molecules in a species-independent manner. The Examiner also acknowledged in the interview that Hug et al. does not teach attaching label-tags to two distinct target nucleic acids molecules as claimed in claim 39. Applicants respectfully assert that Hug et al. as cited by the Examiner in the office action does not disclose the claim 26 as presently amended or claim 39 as previously presented. Accordingly, for the reasons set forth above, withdrawal of the rejection of claims 26, 29, and dependent claims therefrom under 35 U.S.C. 103(a) is respectfully requested.

103(a) Rejection of claims 1-4, 6, 17-24 and 26-48

Claims 1-4, 6, 17-24 and 26-48 are rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over Hug et al. (Hug) in view of U.S. Patent No. 5,648,245 (USPAT '245).

Without conceding the validity of the rejection, and solely to expedite prosecution, Applicants have cancelled claims 1-4, 6, 17-24 and 31-38 and have amended claim 26 to recite "(a) attaching by a species-independent manner to each occurrence of the first target molecule a label from a set of diverse labels." For the reasons cited above, Hug et al. does not teach labeling molecules in a species-independent manner nor attaching label-tags to two distinct nucleic acid molecules. Applicants respectfully assert that none of the references cited by the Examiner in the office action discloses the claim 26 as presently amended or claim 39 as previously presented. Accordingly, for the reasons set forth above, withdrawal of the rejection of claims 26, 29, and dependent claims therefrom under 35 U.S.C. 103(a) is respectfully requested.

103(a) Rejection of claims 1-4, 6, 17-23 and 25-48

Claims 1-4, 6, 17-23 and 25-48 are rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over Hug et al. (Hug) in view of Walker et al. (Walker).

Without conceding the validity of the rejection, and solely to expedite prosecution, Applicants have cancelled claims 1-4, 6, 17-23, 25 and 31-38 and have amended claim 26 to recite

"(a) attaching by a species-independent manner to each occurrence of the first target molecule a label from a set of diverse labels." For the reasons cited above, Hug et al. does not teach labeling molecules in a species-independent manner nor attaching label-tags to two distinct nucleic acid molecules. Applicants respectfully assert that none of the references cited by the Examiner in the office action discloses the claim 26 as presently amended or claim 39 as previously presented. Accordingly, for the reasons set forth above, withdrawal of the rejection of claims 26, 29, and dependent claims therefrom under 35 U.S.C. 103(a) is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Further, the Commissioner is hereby authorized to charge any additional fees or credit any overpayment in connection with this paper to Deposit Account No. 23-2415 (Docket No. 41977-701.201).

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at (858) 350-2365.

Respectfully submitted,

Dated: 3/4/14

/Lucia Muntean/
Lucia Muntean
Reg. No. 69,481

650 Page Mill Road
Palo Alto, CA 94304
(650) 493-9300
Customer No. 021971

EXHIBIT B

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
12/969,581	12/15/2010	Stephen P.A. Fodor	41977-701.201	4473

21971 7590 10/03/2013

WILSON, SONSINI, GOODRICH & ROSATI
650 PAGE MILL ROAD
PALO ALTO, CA 94304-1050

EXAMINER	
MAHATAN, CHANNING S	
ART UNIT	PAPER NUMBER
1636	
MAIL DATE	DELIVERY MODE
10/03/2013	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 12/969,581	Applicant(s) FODOR ET AL.	
	Examiner CHANNING S. MAHATAN	Art Unit 1636	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 July 2013*.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1-10 and 17-48* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1-10 and 17-48* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☒ The drawing(s) filed on *15 December 2010* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a)☐ All b)☐ Some * c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

4) ☐ Other: _____.

Continuation of Attachment(s) 2). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date : 04/12/2013; 07/10/2012; 07/26/2011.

DETAILED ACTION

Response to Restriction Requirement

The election without traverse of Invention I (claims 1-10 and 17-48, drawn to a method of determining (estimating, counting, quantifying) a number of target molecules in a sample) in the '*Response to Restriction Requirement'*, filed on July 19, 2013, is acknowledged.

Accordingly, the requirement is deemed proper and is therefore made FINAL.

Claims under Examination

Claims 11-16 have been canceled.

Accordingly, claims herein under examination are claims 1-17 and 17-48.

Information Disclosure Statement

The '*Information Disclosure Statements*', filed on April 12, 2013; July 10, 2012; and July 26, 2011, have been fully considered. The Hollas reference cited in the '*Information Disclosure Statement*', filed on April 12, 2013, is illegible and appears in duplicate to that found in the '*Information Disclosure Statement*', filed on July 26, 2011. Accordingly, the Hollas reference cited in the '*Information Disclosure Statement*', filed on April 12, 2013, has been lined through.

Claim Rejections - 35 USC § 112(b)

The following is a quotation of 35 U.S.C. 112(b):

> (b) CONCLUSION.—The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the inventor or a joint inventor regards as the invention.

The following is a quotation of 35 U.S.C. 112 (pre-AIA), second paragraph:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5 and 7-10 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor, or for pre-AIA the Applicant regards as the invention.

Lack of Antecedent Basis

Claim 5 recites the limitation "the expected number of target molecules" which lacks proper antecedent basis. Claim 1, which claim 5 directly depends from, does not provide an indication/recitation of an expected number of target molecules. In the absence of a recitation for an expected number of target molecules the determination of a number of different labels to be at least an order of magnitude larger than the expected number of target molecules is incalculable. Accordingly, clarification and appropriate correction is requested.

Claims 7-10 recites the limitation "the ratio of target molecule occurrences to number of different labels" which lacks proper antecedent basis. Claim 1, which claims 7-10 directly depend from, does not provide for either a "target of molecule occurrences" or a "number of different labels" such that a ratio may be determined. In the absence of a recitation for both a for either a "target of molecule occurrences" or a "number of different labels" a ratio is incalculable. Accordingly, clarification and appropriate correction is requested.

Claim Rejections - 35 USC § 103

The following is a quotation of pre-AIA 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under pre-AIA 35 U.S.C. 103(a), the Examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the Examiner to consider the applicability of pre-AIA 35 U.S.C. 103(c) and potential pre-AIA 35 U.S.C. 102(e), (f) or (g) prior art under pre-AIA 35 U.S.C. 103(a).

Hug et al.

Claims 1-4, 6, 17-23, and 26-48 are rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over Hug et al. (Measurement of the Number of Molecules of a Single mRNA Species in Complex mRNA Preparation. 2003. Journal of Theoretical Biology. Vol. 221, pages 615-624; see '*Information Disclosure Statement*', filed on July 10, 2012; herein "Hug").

The instant specification provides the following with respect to stochastic labeling:

> "New methods and compositions for single molecule counting employing the use of stochastic labeling are disclosed herein. In preferred aspects, a diverse set of labels is randomly attached to a population of identical molecules is converted into a population of distinct molecules suitable for threshold detection. Random attachment as used herein refers to a process whereby any label can be attached to a given molecule with the same probability. To demonstrate stochastic labeling methods experimentally the absolute and relative number of selected genes were determined after stochastically labeling 360,000 different fragments of the human genome. The approach does not require the physical separation of molecules and may take advantage of highly parallel methods such as microarray and sequencing technologies to simultaneously count absolute numbers of multiple targets. In some embodiments,

> stochastic labeling may be used for determining the absolute number of RNA or DNA molecules within single cells." (paragraph bridging pages 41 & 42)

Thus, it reasonably understood by one of ordinary skill in the art that stochastic labeling refer to the random labeling/attachment of a population of identical molecules in order to convert the population into distinct molecules for detection/counting.

Hug describes a method of calculating the number of molecules in a single nucleic acid (e.g., mRNA) species in a complex nucleic acid (e.g., mRNA) preparation, wherein individual molecules pertaining to the same molecular species are transformed into mixture of new different molecular species and amplified (Abstract).

Regarding claims 1, 17, 18, 21, 26, 31, 39, and 40 ("[a] method… comprising: (a) combining the sample with a collection of labels, wherein the collection of labels comprises multiple copies of each of a plurality of different label sequences; (b) attaching labels to molecules in a stochastic manner to obtain label-target molecules… and (e) counting the number of different label-target features that are labeled for each different target, wherein the count for each different target is the estimate of the number of occurrences of that target in the sample", "[a] method… comprising…", "… labeling each target polynucleotide in the sample so that substantially every target polynucleotide is associated with a unique oligonucleotide tag- label, each oligonucleotide tag-label comprising an identification tag; separating the tagged target polynucleotides from the non-target polynucleotides in the sample and determining the number of different oligonucleotide tags that are attached to each type of target polynucleotide in the sample by determining the number of different identification tag-labels that are attached to target polynucleotides; and determining the number of target polynucleotides from the number of

different oligonucleotide tags in the sample", "... providing for each target polynucleotide a plurality of nucleic acid probes specific for the target polynucleotide, each nucleic acid probe having a different oligonucleotide tag; combining in a reaction mixture the plurality of nucleic acid probes with the target polynucleotides so that substantially every target polynucleotide associates with a nucleic acid probe to form a probe-target complex, the plurality of nucleic acid probes having a number sufficiently greater than the number of target polynucleotides so that substantially every probe-target complex has a unique oligonucleotide tag; treating the sample to enrich the probe-target complexes...", "... labeling by sampling each target polynucleotide in the mixture so that substantially every target polynucleotide has an oligonucleotide label ligated thereto...", "... attaching to each occurrence of the first target molecule a label from a set of diverse labels wherein said set comprises m different labels, thereby generating for each occurrence of the first target molecule, a new molecule that comprises a copy of the first target molecule and a label, wherein more than 90% of the new molecules have a label that is different from the labels on the other new molecules; detecting each new molecule by detecting each label present on a new molecule; and counting the number of new molecules, thereby counting the number of molecules of the first target molecule in the sample", "... (a) providing a sample comprising a plurality of target nucleic acid molecules, wherein said plurality of target nucleic acid molecules comprises at least two different target nucleic acid molecules; (b) transforming within said sample by a stochastic process said target nucleic acid molecules to produce transformed target nucleic acid molecules... and (d) counting said target nucleic acid molecules by detecting copies of said transformed target nucleic acid molecules to determine an absolute count of occurrences of said target nucleic acid molecules in said sample, wherein detecting said

one or more copies of said transformed target nucleic acid molecules comprises detecting at least a portion of a sequence of one of said target nucleic acid molecules, its complement, or its reverse complement", "… (a) combining a mixture comprising at least two distinct target nucleic acid molecules with a pool of nucleic acid label-tags, wherein said pool of nucleic acid label-tags comprises a plurality of nucleic acid label-tags with different sequences; (b) attaching at least two of said nucleic acid label-tags from said pool of nucleic acid label-tags to at least two of said distinct target nucleic acid molecules to obtain at least two label tag-target nucleic acid molecules, wherein said distinct target nucleic acid molecules have different sequences from one another… and (d) detecting…", "attaching is stochastic"), Hug provides for estimating/counting/determining the number of individual molecules pertaining to the same molecular species in a complex molecular sample and describes two approaches (page 3, 4th full paragraph to page 4, 2nd full paragraph). In the first approach, molecular species are targeted for random labeling with an oligonucleotide tag, wherein Hug states:

> "The first approach is based on a method for cloning tagged nucleic acid molecules onto the surface of micro-beads (Brenner *et al.*, 2000*b*). A tag consists of eight 4mers (blocks). To minimize cross-hybridization between tags and between mRNA molecules and tags, the number of 4mers used is restricted to eight (out of 256). During construction of the tags, one of the eight 4mers is selected for each block. The number of different tags that can be build in this way is approximately $1{:}6 \cdot 10^7$ (Brenner *et al.*, 2000*b*).
>
> We suggest to randomly attach a tag to each IMPSMS in order to generate a new DMS. If the number of tags is sufficiently large a unique tag will be attached to each IMPSMS and the number of new DMS is equivalent to the number of IMPSMS in the original sample. Each new DMS is uniquely defined by its tag sequence. In a final step the number of different tag sequences is determined. We consider two methods depending on the expected number of IMPSMS. If the number of required tag sequences is less than 60000, the new DMS molecules are hybridized onto the surface of beads for further DNA sequencing, using the massively parallel signature sequencing (MPSS) method (Brenner *et al.*, 2000*a*). For still smaller numbers, the sequencing can be avoided and the molecules are hybridized onto an addressable chip surface containing molecules with reverse complementary tag sequences. If the number of required tag sequences exceeds 60000, the new DMS could be analysed by defined block selection as introduced below. Using this method in principle up to 10^6 IMPSMS can be detected." (paragraph bridging pages 3 & 4 to page 4, 1st full paragraph)

In the second approach, molecular species are targeted by random addition of a variable number of short oligonucleotide linkers, wherein Hug states:

> "The second approach to transform IMPSMS into new DMS is based on linker ligation. Short oligonucleotide linkers are mixed with a certain ratio of oligonucleotide terminators and are added to the IMPSMS preparation. At each IMPSMS a random number of oligonucleotide linkers will be added until elongation is terminated by adding an oligonucleotide terminator. New DMS are defined by the number of linkers attached to each IMPSMS. The length of the originating DMS can be determined (by gel electrophoresis), where we expect to be able to distinguish up to 1000 different linker lengths." (page 4, 2nd full paragraph)

Hug indicates each target nucleic acid will be combined with a unique tag (paragraph bridging pages 5 & 6).

Regarding claims 1, 3, 21-23, 31, and 39 ("...(c) optionally amplifying the label-target molecules...", "prior to the hybridizing step (d) the label- target molecules are amplified by PCR so that there are a plurality of copies of each label-target molecule that are hybridized to the array of probes", "... amplifying the oligonucleotide labels that are ligated to target polynucleotides... ", "the step of amplifying comprises PCR", "the step of amplifying comprises reverse transcription", "... (c) amplifying within said sample said transformed target nucleic acid molecules to produce copies of said transformed target nucleic acid molecules...", "... (c) amplifying at least a portion of said label-tag-target nucleic acid molecules, wherein an amplified portion of said label-tag-target nucleic acid molecules comprises at least a portion of said target nucleic acid molecule..."), Hug provides for PCR amplification of the label-target molecule for subsequent hybridization with oligonucleotide chips (Abstract; page 5, 2nd full paragraph; page 9, 2nd full paragraph; and page 12, 2nd full paragraph).

Regarding claims 1, 18, 21, and 46-48 ("... (d) hybridizing the label-target molecules to an array of probes comprising a plurality of features wherein each feature contains a different probe sequence and the probe sequence in each feature is specific for a different label-target

combination, wherein the array comprises a plurality of label/target features for each of a plurality of targets…", "determining the number of different oligonucleotide tags in a sample of enriched probe-target complexes by hybridization thereby determining the number of target polynucleotide in the mixture", "… determining the number of different oligonucleotide labels... by hybridization…", "detecting comprises hybridizing at least a portion of said label-tag-target nucleic acid molecules to a solid or semi-solid substrate", "hybridizing comprises hybridizing at least a portion of said target nucleic acid molecule to a solid or semi-solid substrate", "hybridizing comprises hybridizing at least a portion of said nucleic acid label-tag to a solid or semi-solid substrate"), Hug provides for hybridization to an addressable chip surface (e.g., solid or semi-solid substrate) (page 4, 1st full paragraph; page 9, 4th full paragraph; and page 12, 1st full paragraph; and page 13, 2nd full paragraph).

Regarding claims 2 and 27-30 ("the collection of labels comprises a number of different label sequences that is at least twice the number of each target molecule to be estimated", "the ratio of m to n is greater than 50", "… greater than 100", "…greater than 500", "…greater than 1000"), Hug describes the calculation of the estimated tag/label to target (e.g., ratio), wherein there are at least twice the number of labels to target (e.g., approximately 500 and 50000 for 10^5 and 10^6, respectively) (page 6, 1st & 2nd paragraphs).

Regarding claims 4, 19, 20, 37, and 38 ("a genomic DNA sample comprises the target molecules, said method further comprising: fragmenting the genomic DNA sample to obtain fragments comprising target molecules, ligating a first adaptor comprising a common priming sequence is ligated to a first end of the fragments and a second adaptor comprising a label and a second common priming sequence is ligated to the second end of the fragments, wherein the

label sequence is variable and the second common priming sequence is constant, and wherein the label is situated between the target fragment and the second common priming sequence, thereby obtaining adaptor-ligated, labeled fragments; amplifying said adaptor-ligated, labeled fragments by PCR using a primer or a pair of primers to the first and second common priming sequences; and thereby obtaining amplified labeled targets", "the target polynucleotide is a restriction fragment having a first single strand sequence overhang and a second, different single strand overhang, and wherein a first adaptor has a single stranded overhang that is perfectly complementary to the first overhang and a second different adaptor has a single stranded overhang that is perfectly complementary to the second overhang", "the restriction fragment is formed by digesting genomic DNA with at least one restriction endonuclease", "transforming comprises fragmenting said target nucleic acid molecules", "transforming comprises attaching a label to said target nucleic acid molecules"), Hug describes multimeric linker labeling and depicts the digestion of nucleic acids with a restriction enzyme (e.g., BamH1) (e.g., fragmenting), subsequent ligation with a first and second adaptor the binding of adaptors, and PCR amplification (paragraph bridging pages 10 & 11; and Figure 3A).

Regarding claim 6 ("labels are attached to targets by ligation"), Hug provides for label attachment to targets by ligation (page 4, 2nd full paragraph).

Regarding claims 32 and 33 ("counting is substantially independent of amplification efficiency", "counting is substantially independent of a normalization process"), Hug resolves the issue pertaining to data normalization and indicates the methods proposed relies on the transformation of the quantitative problem into a qualitative problem (e.g., independent of amplification efficiency and normalization process (Abstract; page 3, 4th full paragraph).

Regarding claim 34 ("target nucleic acid molecules comprise sequences from different genomic regions from one another"), Hug provides for the determination of nucleic acid molecules in a complex nucleic acid mixture (page 16, 1st full paragraph; and Figure 1).

Regarding claims 35 and 36 ("copies from substantially all of said transformed target nucleic acid molecules are counted", "only a subset of the copies from said transformed target nucleic acid molecules are counted"), Hug provides for the counting of the number of individual molecules in a complex molecular sample (page 3, 4th full paragraph; and page 5, 1st full paragraph).

Regarding claims 41 and 42 ("target nucleic acid molecules are known targets", "nucleic acid label-tags are designed to bind to said particular nucleic acid target molecules"), Hug provides for the utilization of oligonucleotides that target known sequences (page 10, 2nd full paragraph; Figures 3B & 3C).

Regarding claim 43 ("an identity of said target nucleic acid molecules is determined after the detecting step"), Hug provides for distinguishing target nucleic acid molecule by gel electrophoresis, or labeling and separation, or DNA sequencing methods (page 5, 2nd full paragraph).

Regarding claim 44 ("said nucleic acid label-tags will bind to any of said target nucleic acid molecules"), Hug indicates every target nucleic acid will be combined with a unique tag (paragraph bridging pages 5 & 6).

Regarding claim 45 ("attaching occurs on both ends of at least one of said target nucleic acids"), Hug indicates attachment of at primer binding sites at the 5' and 3' ends (page 10, 2nd full paragraph; and Figures 3A-C).

In view of the teachings of Hug (as stated above), it would have been obvious to one of ordinary skill in the art at the time the invention was made to have applied the theoretical approach for counting individual molecules as described by Hug into attempt the theory in practice, since Hug provides one of ordinary skill in the art some teaching, suggestion, or motivation to extend such theory into practice by stating:

> "In principle, our strategies provide a very accurate method for measuring the expression of defined candidate genes involved in diseases." (page 623, left column, 2nd full paragraph).

Accordingly, Hug renders the instant claims unpatentable.

Hug et al. further in view of U.S. Patent No. 5,648,245

Claims 1-4, 6, 17-24, and 26-48 are rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over Hug et al. (Measurement of the Number of Molecules of a Single mRNA Species in Complex mRNA Preparation. 2003. Journal of Theoretical Biology. Vol. 221, pages 615-624; see '*Information Disclosure Statement*', filed on July 10, 2012; herein "Hug") as applied to claims 1-4, 6, 17-23, and 26-48 above, further in view of U.S. Patent No. 5,648,245 (see attached '*PTO-892*'; herein "USPAT '245").

Hug et al. is herein applied from the above '*103 Rejection*'. However, Hug fails to specifically teach amplification by rolling circle amplification. USPAT '245 resolves the deficiencies of Hug, wherein USPAT '245 discloses a method for constructing an oligonucleotide library (Abstract, Col. 1, lines 13-20).

Regarding claim 24 ("the step of amplifying comprises rolling circle amplification"), USPAT '245 describes rolling circle replication (e.g., rolling circle amplification) (Col. 2, lines 24-51).

In view of the teachings of Hug and USPAT '245 (as stated above), it would have been obvious to one of ordinary skill in the art at the time the invention was made to have alternatively applied other amplification methods, such as rolling circle replication/amplification, for counting individual molecules as described by Hug, since USPAT '245 provides one of ordinary skill in the art some teaching, suggestion, or motivation to apply rolling circle replication/amplification to templates on the order of kilobases and larger (Col. 2, lines 42-44).

Accordingly, Hug further in view of USPAT '245 renders the instant claims unpatentable.

Hug et al. further in view of Walker et al.

Claims 1-4, 6, 17-23, and 25-48 are rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over Hug et al. (Measurement of the Number of Molecules of a Single mRNA Species in Complex mRNA Preparation. 2003. Journal of Theoretical Biology. Vol. 221, pages 615-624; see '*Information Disclosure Statement*', filed on July 10, 2012; herein "Hug") as applied to claims 1-4, 6, 17-23, and 26-48 above, further in view of Walker et al. (Isothermal *in vitro* amplification of DNA by a restriction enzyme/DNA polymerase system. January 1992. Proceedings of the National Academy of Science USA. Vol. 89, pages 392-396; see attached '*PTO-892*'; herein "Walker").

Hug et al. is herein applied from the above '*103 Rejection*'. However, Hug fails to specifically teach amplification by isothermal amplification. Walker resolves the deficiencies of Hug, wherein Walker describes the development of an isothermal *in vitro* DNA amplification method (Abstract).

Regarding claim 25 ("the step of amplifying comprises an isothermal amplification step using a strand displacing DNA polymerase"), Walker indicates strand displacement amplification as an amplification technique that utilizes readily available enzymes and does not require temperature cycling (page 392, left column, 1st full paragraph). Walker indicates strand displacement is an isothermal alternative for nucleic acid amplification, wherein Walker achieves a 10^6-fold amplification (page 392, right column, 2nd full paragraph).

In view of the teachings of Hug and Walker (as stated above), it would have been obvious to one of ordinary skill in the art at the time the invention was made to have alternatively applied other amplification methods, such as isothermal amplification, for counting individual molecules as described by Hug, since Walker provides one of ordinary skill in the art some teaching, suggestion, or motivation by indicating isothermal amplification (SDA) as alternative amplification technique (page 392, right column, 2nd full paragraph).

Accordingly, Hug further in view of Walker renders the instant claims unpatentable.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Channing S Mahatan whose telephone number is 571-270-7464. The Examiner can normally be reached on Monday - Thursday; 9am-5pm.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Anne M. Gussow can be reached on 571-272-6047. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CHANNING S MAHATAN
Examiner
Art Unit 1636

/Channing S Mahatan/
Examiner, Art Unit 1636

/Anne M. Gussow/
Supervisory Patent Examiner, Art Unit 1636

EXHIBIT C

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
12/969,581	12/15/2010	Stephen P.A. Fodor	41977-701.201	4473

21971 7590 03/06/2014

WILSON, SONSINI, GOODRICH & ROSATI
650 PAGE MILL ROAD
PALO ALTO, CA 94304-1050

EXAMINER	
MAHATAN, CHANNING S	
ART UNIT	PAPER NUMBER
1636	

NOTIFICATION DATE	DELIVERY MODE
03/06/2014	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentdocket@wsgr.com

Applicant-Initiated Interview Summary	Application No.	Applicant(s)	
	12/969,581	FODOR ET AL.	
	Examiner	Art Unit	
	CHANNING S. MAHATAN	1636	

All participants (applicant, applicant's representative, PTO personnel):

(1) *Channing S Mahatan*.

(2) *Anne M. Gussow*.

(3) *Vern Norviel*.

(4) *Stephen P.A. Fodor*.

Date of Interview: *27 February 2014*.

Type: ☐ Telephonic ☐ Video Conference
☒ Personal [copy given to: ☒ applicant ☒ applicant's representative]

Exhibit shown or demonstration conducted: ☐ Yes ☒ No.
If Yes, brief description: _____.

Issues Discussed ☐101 ☐112 ☐102 ☒103 ☐Others
(For each of the checked box(es) above, please describe below the issue and detailed description of the discussion)

Claim(s) discussed: *26 and 39*.

Identification of prior art discussed: *Hug et al.*.

Substance of Interview
(For each issue discussed, provide a detailed description and indicate if agreement was reached. Some topics may include: identification or clarification of a reference or a portion thereof, claim interpretation, proposed amendments, arguments of any applied references etc...)

Applicant, Stephen P.A. Fodor, and Applicant's Representative, Vern Norviel, presented claim amendments and arguments. However, further consideration and search would be required.

Applicant recordation instructions: The formal written reply to the last Office action must include the substance of the interview. (See MPEP section 713.04). If a reply to the last Office action has already been filed, applicant is given a non-extendable period of the longer of one month or thirty days from this interview date, or the mailing date of this interview summary form, whichever is later, to file a statement of the substance of the interview

Examiner recordation instructions: Examiners must summarize the substance of any interview of record. A complete and proper recordation of the substance of an interview should include the items listed in MPEP 713.04 for complete and proper recordation including the identification of the general thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the general results or outcome of the interview, to include an indication as to whether or not agreement was reached on the issues raised.

☒ Attachment

/ANNE GUSSOW/
Supervisory Patent Examiner, Art Unit 1636

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record
A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews
Paragraph (b)

In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR §1.2 Business to be transacted in writing.
All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:
- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:
1) A brief description of the nature of any exhibit shown or any demonstration conducted,
2) an identification of the claims discussed,
3) an identification of the specific prior art discussed,
4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
5) a brief identification of the general thrust of the principal arguments presented to the examiner,
   (The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
6) a general indication of any other pertinent matters discussed, and
7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

EXHIBIT D

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

NOTICE OF ALLOWANCE AND FEE(S) DUE

21971 7590 03/21/2014

WILSON, SONSINI, GOODRICH & ROSATI
650 PAGE MILL ROAD
PALO ALTO, CA 94304-1050

EXAMINER	
MAHATAN, CHANNING S	
ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 03/21/2014

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
12/969,581	12/15/2010	Stephen P.A. Fodor	41977-701.201	4473

TITLE OF INVENTION: Digital Counting of Individual Molecules by Stochastic Attachment of Diverse Labels

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	$960	$0	$0	$960	06/23/2014

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 1/2 the amount of undiscounted fees, and micro entity fees are 1/2 the amount of small entity fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

21971 7590 03/21/2014
WILSON, SONSINI, GOODRICH & ROSATI
650 PAGE MILL ROAD
PALO ALTO, CA 94304-1050

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission
I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
12/969,581	12/15/2010	Stephen P.A. Fodor	41977-701.201	4473

TITLE OF INVENTION: Digital Counting of Individual Molecules by Stochastic Attachment of Diverse Labels

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	$960	$0	$0	$960	06/23/2014

EXAMINER	ART UNIT	CLASS-SUBCLASS
MAHATAN, CHANNING S	1636	506-009000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).
- ❑ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
- ❑ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.
1 _____
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. The following fee(s) are submitted:
- ❑ Issue Fee
- ❑ Publication Fee (No small entity discount permitted)
- ❑ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**
- ❑ A check is enclosed.
- ❑ Payment by credit card. Form PTO-2038 is attached.
- ❑ The Director is hereby authorized to charge the required fee(s), any deficiency, or credits any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)
- ❑ Applicant certifying micro entity status. See 37 CFR 1.29 — NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.
- ❑ Applicant asserting small entity status. See 37 CFR 1.27 — NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.
- ❑ Applicant changing to regular undiscounted fee status. — NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

PTOL-85 Part B (10-13) Approved for use through 10/31/2013. OMB 0651-0033 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
12/969,581	12/15/2010	Stephen P.A. Fodor	41977-701.201	4473

21971 7590 03/21/2014

WILSON, SONSINI, GOODRICH & ROSATI
650 PAGE MILL ROAD
PALO ALTO, CA 94304-1050

EXAMINER	
MAHATAN, CHANNING S	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 03/21/2014

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)

(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 437 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 437 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Notice of Allowability	Application No. 12/969,581	Applicant(s) FODOR ET AL.	
	Examiner CHANNING S. MAHATAN	Art Unit 1636	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *04 March 2014*.
   ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on_____.
2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.
3. ☒ The allowed claim(s) is/are *26-30 and 39-138*. As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov .
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

   Certified copies:

   a) ☐ All b) ☐ Some *c) ☐ None of the:
   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
4. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
5. ☐ Examiner's Amendment/Comment
6. ☒ Examiner's Statement of Reasons for Allowance
7. ☐ Other _____.

/ANNE GUSSOW/
Supervisory Patent Examiner, Art Unit 1636

The present application is being examined under the pre-AIA first to invent provisions.

DETAILED ACTION

Response to Non-Final Office Action

The '*Response to Non-Final Office Action*', filed on March 04, 2014, has been fully considered.

Status of Claims

Claims 1-25 and 31-38 have been canceled.

Claims 26 and 39-48 have been amended.

Claims 49-138 have been added and are deemed to be directed to examined Invention I, drawn to a method of determining (estimating, counting, quantifying) a number of target molecules in a sample.

Accordingly, claims 26-30 and 39-138 are pending.

Reasons for Allowance

The following is an Examiner's statement of reasons for allowance:

- The most relevant identified prior art reference is Hug et al. (Measurement of the Number of Molecules of a Single mRNA Species in Complex mRNA Preparation. 2003. Journal of Theoretical Biology. Vol. 221, pages

615-624; see '*Information Disclosure Statement*', filed on July 10, 2012; herein "Hug"). Hug describes a method of calculating the number of molecules in a single nucleic acid (e.g., mRNA) species in a complex nucleic acid (e.g., mRNA) preparation, wherein individual molecules pertaining to the same molecular species are transformed into mixture of new different molecular species and amplified (Abstract). However, Hug fails to teach or suggest "attaching by a species-independent manner to each occurrence of the first target molecule a label from a set of diverse labels" and/or "attaching label-tags to two distinct target nucleic acid molecules."

- The claim amendments found in the '*Response to Non-Final Office Action*', filed on March 04, 2014, has overcome all grounds of rejection in the '*Non-Final Office Action*', mailed October 03, 2013. No other grounds for rejection are present.
- No pending United States applications have been identified with claims directed to the same invention as claimed herein.
- Therefore, claims 26-30 and 39-138 are deemed allowable.

Any comments considered necessary by Applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Channing S Mahatan whose telephone number is 571-270-7464. The Examiner can normally be reached on Monday - Thursday; 9am-5pm.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Anne M. Gussow can be reached on 571-272-6047. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CHANNING S MAHATAN
Examiner
Art Unit 1636

/Channing S Mahatan/
Examiner, Art Unit 1636

/ANNE GUSSOW/
Supervisory Patent Examiner, Art Unit 1636

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	12969581	FODOR ET AL.
	Examiner	**Art Unit**
	CHANNING S MAHATAN	1636

CPC						
Symbol					**Type**	**Version**
			/			
			/			
			/			
			/			
			/			
			/			
			/			
			/			
			/			
			/			
			/			
			/			
			/			
			/			
			/			

CPC Combination Sets							
Symbol					**Type**	**Set**	**Ranking**	**Version**
			/					
			/					

/CHANNING S MAHATAN/ Examiner.Art Unit 1636	03/14/2014	**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	105	
/ANNE GUSSOW/ Supervisory Patent Examiner.Art Unit 1636	03/17/2014	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	NONE

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	12969581	FODOR ET AL.
	Examiner	**Art Unit**
	CHANNING S MAHATAN	1636

US ORIGINAL CLASSIFICATION		INTERNATIONAL CLASSIFICATION												
CLASS	SUBCLASS	CLAIMED					NON-CLAIMED							
506	9	C	4	0	B	30 / 04 (2006.01.01)								
CROSS REFERENCE(S)		C	1	2	Q	1 / 68 (2006.01.01)								
CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)													
435	6.1													

/CHANNING S MAHATAN/ Examiner.Art Unit 1636	03/14/2014	**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	105	
/ANNE GUSSOW/ Supervisory Patent Examiner.Art Unit 1636	03/17/2014	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	NONE

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	12969581	FODOR ET AL.
	Examiner	**Art Unit**
	CHANNING S MAHATAN	1636

☒ **Claims renumbered in the same order as presented by applicant** ☐ **CPA** ☐ **T.D.** ☐ **R.1.47**

Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original
	1		20	6	39	25	58	44	77	63	96	82	115	101	134
	2		21	7	40	26	59	45	78	64	97	83	116	102	135
	3		22	8	41	27	60	46	79	65	98	84	117	103	136
	4		23	9	42	28	61	47	80	66	99	85	118	104	137
	5		24	10	43	29	62	48	81	67	100	86	119	105	138
	6		25	11	44	30	63	49	82	68	101	87	120		
	7	1	26	12	45	31	64	50	83	69	102	88	121		
	8	2	27	13	46	32	65	51	84	70	103	89	122		
	9	3	28	14	47	33	66	52	85	71	104	90	123		
	10	4	29	15	48	34	67	53	86	72	105	91	124		
	11	5	30	16	49	35	68	54	87	73	106	92	125		
	12		31	17	50	36	69	55	88	74	107	93	126		
	13		32	18	51	37	70	56	89	75	108	94	127		
	14		33	19	52	38	71	57	90	76	109	95	128		
	15		34	20	53	39	72	58	91	77	110	96	129		
	16		35	21	54	40	73	59	92	78	111	97	130		
	17		36	22	55	41	74	60	93	79	112	98	131		
	18		37	23	56	42	75	61	94	80	113	99	132		
	19		38	24	57	43	76	62	95	81	114	100	133		

/CHANNING S MAHATAN/ Examiner.Art Unit 1636 (Assistant Examiner)	03/14/2014 (Date)	**Total Claims Allowed:** 105	
/ANNE GUSSOW/ Supervisory Patent Examiner.Art Unit 1636 (Primary Examiner)	03/17/2014 (Date)	O.G. Print Claim(s) 1	O.G. Print Figure NONE